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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/037,299	10/25/2001	Stewart Thomas Leslie	208.1009	4506

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EXAMINER	
OH, SIMON J	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
08/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/037,299	LESLIE, STEWART THOMAS	
	Examiner	Art Unit	
	Simon J. Oh	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 5-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 5-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All. b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Papers Received

Receipt is acknowledged of the applicant's response, received on 07 May 2007.

Withdrawal of Finality

Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The rejection of Claims 1, 2 and 5-19 under 35 U.S.C. 102(b) over Granger *et al.* is hereby withdrawn in view of the applicant's present response.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 2, and 5-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Granger *et al.* (U.S. Patent No. 5,149,538) in view of Blum *et al.* (U.S. Patent No. 5,891,919)

The Granger *et al.* patent teaches a transdermal dosage form that is formulated to be resistant to abuse by ingestion or solvent immersion (See Abstract). The dosage form may

comprise an opioid, such as buprenorphine, hydromorphone, morphine, and fentanyl (See Column 4, Lines 36). An opioid antagonist such as naloxone is also included to prevent misuse of the dosage form (See Column 5, Lines 26-38). The antagonist is released from the dosage form when it is ingested or immersed in a solvent for the purpose of attenuating the euphoric effect of the opioid (See Column 2, Lines 40-46; and Column 3, Lines 32-37). A variety of permeation enhancers may be incorporated into the dosage form (See Column 4, Line 63 to Column 5, Line 25). Various embodiments of the disclosed invention include the use of an adhesive matrix containing the opioid, the use of a barrier means to separate the antagonist from the opioid, and the use of a soluble material that encapsulates discrete units of the antagonist (See Column 4, Lines 11-27; and Column 6, Lines 3-19).

The Granger *et al.* patent does not teach the use of an emetic, nauseant, flavoring substance, ergolide, bitter quaternary ammonium compound, or atropine as a distressing agent in a transdermal formulation of an opioid analgesic.

The Blum *et al.* patent teaches the use of denatonium capsaicinate as a substance providing a bitter and/or spicy flavor for use as an aversive agent (See Abstract). It may be incorporated into topical formulations and dressings and other pharmacological compositions (See Column 4, Lines 38-47).

It would be obvious to one of ordinary skill in the art to combine the two prior art references in order to obviate the instantly claimed invention. The Granger *et al.* patent teaches a transdermal formulation which provides the benefit of an opioid analgesic with the additional feature of a means to prevent abuse by ingestion or solvent extraction. One of ordinary skill in the art would recognize that because the means to prevent abuse is put into effect upon an

attempt by a subject to ingest the active agent in the dosage form taught by Granger *et al.*, it logically follows that other agents that trigger an aversive response upon ingestion or attempted ingestion may be substituted as an equivalent. Thus, one of ordinary skill in the art would know that the agent described by Blum *et al.* would be a suitable substitute, since it is also intended for use in topical formulations, dressings, and other pharmacological compositions. The result that is reasonably predicted by one of ordinary skill in the art is the formulation of a transdermal dosage form containing an opioid analgesic and denatonium capsaicinate that produces an aversive response when a subject attempts to abuse the dosage form by ingestion. By extension, the constituent components of denatonium capsaicinate, which are denatonium benzoate and capsaicin and are also described by Blum *et al.*, would also be seen by one of ordinary skill in the art as acceptable substitutes, since each of these constituent substances serve the same purpose of producing an aversive response upon ingestion. Therefore, the instantly claimed invention is *prima facie* obvious.

Claims 1, 2, and 5-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Granger *et al.* (U.S. Patent No. 5,149,538) in view of Porter (U.S. Patent No. 4,175,119).

The Granger *et al.* patent teaches a transdermal dosage form that is formulated to be resistant to abuse by ingestion or solvent immersion (See Abstract). The dosage form may comprise an opioid, such as buprenorphine, hydromorphone, morphine, and fentanyl (See Column 4, Lines 36). An opioid antagonist such as naloxone is also included to prevent misuse of the dosage form (See Column 5, Lines 26-38). The antagonist is released from the dosage form when it is ingested or immersed in a solvent for the purpose of attenuating the euphoric

effect of the opioid (See Column 2, Lines 40-46; and Column 3, Lines 32-37). A variety of permeation enhancers may be incorporated into the dosage form (See Column 4, Line 63 to Column 5, Line 25). Various embodiments of the disclosed invention include the use of an adhesive matrix containing the opioid, the use of a barrier means to separate the antagonist from the opioid, and the use of a soluble material that encapsulates discrete units of the antagonist (See Column 4, Lines 11-27; and Column 6, Lines 3-19).

The Granger *et al.* patent does not teach the use of an emetic, nauseant, flavoring substance, ergolide, bitter quaternary ammonium compound, or atropine as a distressing agent in a transdermal formulation of an opioid analgesic.

The Porter patent teaches the use of an emetic to prevent accidental or intentional overdose of a psychoactive substance (See Abstract; and Column 1, Lines 40-43). Such emetic substances include emetine hydrochloride, ipecamine, hydro-ipecamine, and ipecacuanhic acid (See Column 1, Lines 52-57). It may be incorporated into formulations containing narcotic analgesics such as hydromorphone and codeine (See Column 3 Lines 55-57).

It would be obvious to one of ordinary skill in the art to combine the two prior art references in order to obviate the instantly claimed invention. The Granger *et al.* patent teaches a transdermal formulation which provides the benefit of an opioid analgesic with the additional feature of a means to prevent abuse by ingestion or solvent extraction. One of ordinary skill in the art would recognize that because the means to prevent abuse is put into effect upon an attempt by a subject to ingest the active agent in the dosage form taught by Granger *et al.*, it logically follows that other agents that trigger an aversive response upon ingestion or attempted ingestion may be substituted as an equivalent. Thus, one of ordinary skill in the art would know

that the emetics described by Porter would be a suitable substitute, since it is also intended for use with narcotic analgesics, to prevent their overdose. The result that is reasonably predicted by one of ordinary skill in the art is the formulation of a transdermal dosage form containing an emetic that produces an aversive response when a subject attempts to abuse the dosage form by ingestion. As emetine hydrochloride, ipecamine, hydro-ipecamine, and ipecacuanhic acid are substances (or derivatives thereof) that are found in the ipecacuanha plant, claim limitations drawn to the use of ipecacuanha are met by the collective disclosure of the prior art. Therefore, the instantly claimed invention is *prima facie* obvious.

Response to Arguments

Applicant's arguments filed 23 October 2006 have been considered but are moot in view of the new grounds for rejection set forth above.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Simon J. Oh whose telephone number is (571) 272-0599. The examiner can normally be reached on M-F 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Simon J. Oh
Examiner
Art Unit 1618

sjo

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER